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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(S7) Abstract: This invention provides for a method for inhibiting new tissue growth in blood vessels in a subject, wherein the subject experienced blood vessels injury, which comprises administering to the subject a pharmaceutically effective amount of an inhibitor of receptor for advanced glycation endproduct (RAGE) so as to inhibit new tissue growth in the subject's blood vessels. The invention also provides for method for inhibiting neointimal formation in blood vessels in a subject, wherein the subject experienced blood vessel injury, which comprises administering to the subject a pharmaceutically effective amount of an inhibitor of receptor for advanced glycation endproduct (RAGE) so as to inhibit neointimal formation in the subject's blood vessels. The invention also provides a method for preventing exaggerated restenosis in a diabetic subject which comprises administering to the subject a pharmaceutically effective amount of an inhibitor of receptor for advanced glycation endproduct (RAGE) so as to prevent exaggerated restenosis in the subject.

WO 02/030889 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/32036

A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : A01N 43/04, 63/00; C12N 5/00, 15/00, 15/63 US CL : 514/44; 435/320.1, 325, 455; 424/93.21 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 514/44; 435/320.1, 325, 455; 424/93.21 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched NONE Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST, STN, BIOSIS, MEDLINE, SCISEARCH, CAPLUS		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 00/20458 A1 (THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK) 13 April 200, especially pages 7, 9-11, 44-49.	1-6, 8-9, 11-16
Y	SCHMIDT et al. Activation of Receptor for Advanced Glycation End Products: A Mechanism for Chronic Vascular Dysfunction in Diabetic Vasculopathy and Atherosclerosis. Circulation Research. 19 March 1999, Vol. 84, No. 5, pages 489-497, especially abstract.	1-6, 8-9, 11-16
Y,P	SCHMIDT et al. The Biology of the Receptor for Advanced Glycation End Products and Its Ligands. Biochimica Et Biophysica Acta. 20 December 2000, Vol. 1498, No. 2-3, pages 99-111, see entire document.	1-6, 8-9, 11-16
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "Z" document member of the same patent family		
Date of the actual completion of the international search 11 FEBRUARY 2002		Date of mailing of the international search report 29 APR 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230		Authorized officer SHIN-LIN CHEN Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/32036

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-6, 8-9, 11-16

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/39036

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-6, 8, 9 and 11-16, drawn to a method for inhibiting new tissue growth or inhibiting neointimal formation in blood vessels, or preventing exaggerated restenosis in a diabetic subject by administering to said subject a nucleic acid inhibitor of receptor for advanced glycation endproduct (RAGE).

Group II, claim(s) 1-7 and 11-16, drawn to a method for inhibiting new tissue growth or inhibiting neointimal formation in blood vessels, or preventing exaggerated restenosis in a diabetic subject by administering to said subject an organic or inorganic molecule inhibitor or receptor for advanced glycation endproduct (RAGE).

Group III, claim(s) 1-6, 8, 9 and 11-16, drawn to a method for inhibiting new tissue growth or inhibiting neointimal formation in blood vessels, or preventing exaggerated restenosis in a diabetic subject by administering to said subject a polypeptide inhibitor of receptor for advanced glycation endproduct (RAGE).

Group IV, claim(s) 1-6 and 10-16, drawn to a method for inhibiting new tissue growth or inhibiting neointimal formation in blood vessels, or preventing exaggerated restenosis in a diabetic subject by administering to said subject an antibody inhibitor of receptor for advanced glycation endproduct (RAGE).

Group V, claim(s) 17, 18 and 22-24, drawn to a method for determining whether an organic or inorganic molecule inhibitor inhibits new tissue growth in a blood vessel in a subject by comparing the inhibition of new tissue growth or neointimal formation in said blood vessel in a subject treated or untreated with said organic or inorganic molecule inhibitor.

Group VI, claim(s) 17, 19, 20 and 22-24, drawn to a method for determining whether a nucleic acid inhibitor inhibits new tissue growth in a blood vessel in a subject by comparing the inhibition of new tissue growth or neointimal formation in said blood vessel in a subject treated or untreated with said polypeptide inhibitor.

VII, claim(s) 17, 19, 20 and 22-24, drawn to a method for determining whether a polypeptide inhibitor inhibits new tissue growth in a blood vessel in a subject by comparing the inhibition of new tissue growth or neointimal formation in said blood vessel in a subject treated or untreated with said polypeptide inhibitor.

VIII, claim(s) 17 and 21-24, drawn to a method for determining whether an antibody inhibitor inhibits new tissue growth in a blood vessel in a subject by comparing the inhibition of new tissue growth or neointimal formation in said blood vessel in a subject treated or untreated with said antibody inhibitor.

The inventions listed as Groups I-VIII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I-IV are drawn to different methods using different materials that differ in their chemical compositions and biological functions: nucleic acids, organic or inorganic molecules, polypeptides, and antibodies. The shared technical feature in groups I-IV is receptor for advanced glycation endproduct (RAGE). Schmidt et al., 1999, teaches "Receptor for advanced glycation end products (RAGE) is a member of the immunoglobulin superfamily of cell surface molecules and engages diverse ligands relevant to distinct pathological processes" and "blockade of cell surface RAGE by infusion of a soluble, truncated form of the receptor completely suppressed enhanced formation of vascular lesions." Schmidt also teaches using mice in which RAGE expression has been genetically manipulated and low MW RAGE inhibitor to study the role of RAGE activation in diabetic vasculopathy (e.g. abstract). Thus, groups I-IV do not share a special technical feature and no contribution has been made over the prior art. Groups I-IV are materially different methods that differ in process steps, reagents and dosages used, response variables, and criteria of success. Similarly, groups V-VIII do not share a special technical feature and no contribution has been made over the prior art and are materially different methods that differ in process steps, reagents and dosages used, response variables, and criteria of success.

Groups I-IV are different from groups V-VIII because a method for inhibiting new tissue growth, inhibiting neointimal formation in blood vessels, or preventing exaggerated restenosis is different from a method for determining objectives, process steps, reagents and dosages used, response variables, and criteria of success. Further, the compound used in groups V-VIII encompasses any compound that can inhibit new tissue growth in a blood vessel but not limited to the inhibitor of RAGE that is used in groups I-IV. Thus, groups I-VIII do not relate to a single inventive concept under PCT Rule 13.1